ered as indicating possible hypothyroidism. The attending physician is immediately notified and a sample of serum for a thyroid stimulating hormone (TSH) study is requested. If the TSH level is elevated, a presumptive diagnosis of hypothyroidism is made. In hypothyroid infants a complete study is necessary to determine if the condition is transient or if it is primary hypothyroidism, pituitary or hypothalamic hypothyroidism, a deficiency of thyroxine binding globulin (TBG) or end-organ defect.

There is little question that identification of hypothyroidism in infants is of importance to state and federal governments because of the enormous costs of lifetime care of persons in whom the condition has not been identified. A program of required T_4 testing of newborn infants appears indicated by the significant incidence of this disorder. There is, however, considerable question about the advisability of establishing large government operated laboratories for diagnosis and counseling centers for care. This incursion into private medical practice does not seem needed or justified.

HARRY E. MAAS, MD

REFERENCES

Dussault JH, Morissette J, Letarte J, et al: Modification of a screening program for neonatal hypothyroidism. J Pediatr 92: 274-277, Feb 1978

Mitchel ML, Larsen PR, Levy HL, et al: Screening for congenital hypothyroidism—Results in the newborn population of New England. JAMA 239:2348-2351, Jun 2, 1978

Pap Smears—Lest We Forget

RECENT CRITICISM of cost effectiveness of routine Papanicolaou (Pap) tests has perhaps dampened the enthusiasm of the public, and in some cases physicians, about the need for routine gynecologic Pap tests. There may be value, therefore, in reviewing the history of this simple procedure and its effect on carcinoma of the uterine cervix.

From 1930 to 1974 age-adjusted cancer death rates for females indicated a drop in deaths from cancer of the uterus from first to fourth position, a decrease from 27 per 100,000 females to 8 per 100,000 females. In well-documented studies there has been a pronounced decrease in the cases of invasive cancer. In a 1956 study, 41 percent of the lesions detected were invasive. A 1979 study showed a 9 percent incidence of invasive lesions. From these data it becomes clear that tumors are being detected much earlier and in clinical settings where appropriate treatment for cure is possible. Routine Pap tests undoubtedly contribute to this favorable trend.

On the other hand, mortality data presented in a Minnesota study indicated 66 deaths in 1978 from cervical cancer (Cervical cancer deaths—Minnesota residents 1959-1978. Minneapolis, Minnesota Department of Health Center for Health Statistics, unpublished data). In spite of the widespread use of routine Pap tests, cervical cancer is still very much with us. The factors involved contributing to the continued incidence of death resulting from cancer of the uterine cervix are complex. Included are not carrying out Pap tests or pelvic examinations, inadequate or inappropriate treatment and inadequate follow-up. In 75 percent of the cases, patients are apparently responsible for inadequate care either by refusing pelvic examination or by not visiting a physician for routine annual examination or follow-up examination. In the other 25 percent of the cases physician responsibility was indicated in that pelvic examinations were not done, Pap tests were not carried out, or the reported histologic or cytologic findings were misinterpreted. The need for continued emphasis on physical examination, Pap tests and careful continued follow-up remains clear and cannot be overemphasized.

In recent years, cytology has become more of a diagnostic rather than a screening procedure, and the use of colposcopy in obtaining cervical biopsy specimens when there are abnormal Pap test results has increased the accuracy to approximately 99 percent. There is no excuse which can be justified by lack of *cost effectiveness* to forgive one undetected cancer of the uterine cervix.

RICHARD A. PERRY, MD

REFERENCES

Erickson CC, Everett BE Jr, Graves LM, et al: Population screening for uterine cancer by vaginal cytology—Preliminary summary of results of first examination of 108,000 women and second testing of 33,000 women. JAMA 162:167-173, Sep 15, 1956

Christopherson WM, Parker JE, Drye JC: Control of cervical cancer—Preliminary report on community program. JAMA 182: 179-182, Oct 13, 1962

Christopherson WM, Mendez WM, Ahuja EM, et al: Cervical cancer control in Louiseville, Kentucky. Cancer 26:29-38, Jul 1970

Koss LG: Diagnostic Cytology and Its Histopathologic Bases—Vol 1, 3rd Ed. Philadelphia, J. B. Lippincott, 1979, pp 376-377

Recent Advances in Perinatal Clinical Chemistry

ONE OF THE most important decisions an obstetrician must make is whether or not to let nature take its course and have a baby delivered by natural labor or to preempt nature by inducing delivery. That decision is usually made on the basis of the maternal condition, the health of the fetus and the maturity of the fetus. Recent advances in clinical chemistry have contributed to

our evaluation of fetal health and the maturity. Three specific assays are critical in these evaluations: serum unconjugated estriol, serum human placental lactogen (HPL) and amniotic fluid surfactant measurements.

The serum estriol level is considered a measure of the fetoplacental function. The production of estriol comes about through a rather complex interplay of both fetal and maternal organs. A decreased estriol value, as compared with expected reference values, may often be an indication of a compromised fetus.

Serum HPL values obtained from maternal blood are directly related to placental size. Therefore, pregnancies associated with large placentas, such as in cases of maternal diabetes or multiple gestations (twins, triplets and so forth), will result in high HPL values. Maternal hypertension especially preeclampsia associated with fetal death will often result in very low HPL values. The fetal danger zone (FDZ) has been defined as HPL values in serum below 4 mg per liter after the 30th week of gestation. Many pregnancies associated with hypertension and fetal death will result in HPL values in this FDZ.

While the previously mentioned assays (estriol and HPL) will help an obsetetrician evaluate the health of a fetus, the amniotic fluid surfactant value will give an indication of fetal pulmonary maturity. Two major assays have been used to measure fetal pulmonary maturity: the lecithin to sphingomyelin (L:S) ratio and various foam stability tests. An L:S ratio greater than 2:1 will usually give assurance of fetal pulmonary maturity. The presence of surfactant in amniotic fluid will permit a mixture of amniotic fluid and ethanol to produce foam after being shaken. The presence of foam also gives such assurance of fetal pulmonary maturity. We have found great reliability in a new procedure called the foam stability index (FSI) test. This FSI assay presents the amount of surfactant in terms of the highest ethanol volume fraction which will permit foam to persist after being shaken.

In summary, we find that the serum unconjugated estriol level, serum HPL value and the FSI test result all contribute to a reasonable evaluation of fetal health and maturity. Based on these results and on the status of the pregnant woman, an obstetrician is well equipped to decide whether or not to induce labor or allow nature to take its course. Obviously other paraclinical measurements such as an oxytocin stress test, ultrasound measurements and the like, as well as information gained from a history and physical examination, also will play a role in this decision. Nonetheless, clinical chemistry has contributed much to assisting obstetricians in this decision.

BERNARD E. STATLAND, MD, PhD

REFERENCES

Statland BE, Sher G, Freer DE, et al: Evaluation of a modified foam stability (FS-50) test—An assay performed on amniotic fluid to predict fetal pulmonary maturity. Am J Clin Pathol 69: 514-519, May 1978

Sher G, Statland BE, Freer DE, et al: Assessing fetal lung maturation by the foam stability index test. Obstet Gynecol 52: 673-677, Dec 1978

Immunohistologic Methods in Cell and Tumor Recognition

TRADITIONALLY, recognition of cell types and their corresponding neoplasms is based on the application of time-honored criteria passed down through preceding generations of histopathologists. As a result, the diagnosis of neoplasia is often hedged with uncertainty due to a continuing lack of positive methods with which to validate the morphologic criteria employed.

Cell identification may be enhanced by the use of special staining procedures, such as periodic acid-Schiff, methyl green-pyronine and trichrome stains, though these lack true cellular specificity, or by the application of exacting histochemical techniques that may be specific for cell-based enzymes but are of limited usefulness to diagnostic pathologists because of the requirement for fresh unfixed tissues.

The advent of a labelled antibody technique that is applicable to fixed paraffin embedded tissues thus offers significant advantages because it permits the demonstration of antigenic components within routinely processed material, which is often all that is available to pathologists when the need for special stains becomes apparent.

At present the most widely available of these immunohistologic techniques is based upon the use of horseradish peroxidase as a label for the site of tissue localization of the specific antibody. The specific antibody in turn serves to identify the distribution of the corresponding antigen within the tissue section. The immunoperoxidase technique has much in common with established immunofluorescence methods, with the same advantages of specificity and comparable sensitivity. Morphologic detail is, however, far superior to immunofluorescence and is equivalent to that obtained in routine hemotoxylin-eosin stains of formalin fixed paraffin embedded tissues. Using